

Exercise training and pyridostigmine each have unique benefits for patients with fibromyalgia

Synopsis

Summary of: Jones KD, Burckhardt CS, Deodhar AA, Perrin NA, Hanson GC, Bennett RM (2008) A six-month randomized controlled trial of exercise and pyridostigmine in the treatment of fibromyalgia. *Arthritis & Rheumatism* 58: 612–622. [Prepared by Mark Elkins, CAP Co-ordinator.]

Question: Exercise and the acetylcholine esterase inhibitor, pyridostigmine, increase growth hormone secretion. Do these interventions, alone or in combination, improve pain, tender point count, myalgia scores, and other symptoms in patients with fibromyalgia? **Design:** Randomised, controlled, factorial trial with concealed allocation. **Setting:** A university tertiary care centre in the USA. **Participants:** Adults with fibromyalgia according to American College of Rheumatology criteria. 165 participants were randomised to 4 groups: exercise and pyridostigmine, exercise only, pyridostigmine only, or a control group. **Interventions:** The exercise regimen involved three group exercise sessions per week for 6 months, consisting of aerobic training for 30 min, strength training for 10 min, flexibility training for 5 min, balance training for 5 min, and relaxation for 10 min. The non-exercise groups received weekly telephone calls to discuss dietary intake and a 2-hour monthly visit, intended to control for the effects of staff contact. The pyridostigmine regimen was 60 mg, three times daily, for

6 months. The non-pyridostigmine groups received placebo tablets as a control condition. **Outcome measures:** The primary outcomes were pain measured on a 10 cm visual analogue scale (VAS), the number of tender points, and the total myalgic score. Secondary outcome measures included VAS ratings of fatigue, sleep, stiffness, and anxiety; the Beck Depression Index; the Quality of Life Scale; and clinical tests of flexibility, strength/endurance, and balance. **Results:** 154 participants completed the study. No interaction between the two active interventions was observed. At the end of treatment, neither intervention significantly affected any of the primary outcomes. Exercise significantly improved fatigue, by 1 cm (95% CI 0.3 to 1.7) on the VAS; lower body flexibility, by 4 cm (95% CI 1 to 7) on a seated fingertip-to-toe test; and balance, by 27 sec (95% CI 10 to 42) on a single-leg stance test. Pyridostigmine significantly improved sleep scores, by 1 cm (95% CI 0.3 to 1.8) on the VAS; and anxiety scores, by 1.1 cm (95% CI 0.3 to 2) on the VAS. **Conclusion:** In people with fibromyalgia, exercise improves fatigue, flexibility, and balance, while pyridostigmine improves sleep and anxiety. When both interventions are used simultaneously, both sets of benefits are obtained.

[95% CIs calculated by the CAP Co-ordinator.]

Commentary

Fibromyalgia is characterised by widespread pain, fatigue, stiffness, disrupted sleep, depression, physical deconditioning, and low pain thresholds at specific anatomic sites, which are termed tender points (Wolfe 1990). Exercise or injections of growth hormone can improve fibromyalgia symptoms (Jones 2006, 2007). As a cheaper alternative to injections of growth hormone, the drug pyridostigmine can be used to stimulate the body's growth hormone production. This factorial trial sought to determine the benefits of exercise and pyridostigmine, alone or in combination, in patients with fibromyalgia.

This study is of excellent quality, scoring 9/10 on the PEDro scale (Maher 2003), although the points awarded for blinding apply only to the comparison of pyridostigmine and its placebo. The control condition for the exercise comparison would not successfully blind the exercise, but would at least control for the attention from the investigators. Also, the investigators appropriately lowered the usual significance level to 0.01 to account for the large number of outcomes.

Both this study and the Cochrane systematic review of exercise for fibromyalgia (Busch 2007) found that the effect of exercise on pain was almost statistically significant. If this new study is incorporated in the next update of the review, the new meta-analysis may show that exercise significantly improves pain. Furthermore, the Cochrane review found no data on flexibility and strength, so this study adds important information about these outcomes.

However, the 4 cm improvement in seated fingertip-to-toe distance is of questionable clinical importance.

Pyridostigmine improved a different set of outcomes: sleep and anxiety. These mutually exclusive benefits of the two interventions suggest that both should be offered to fibromyalgia patients. The lack of an interaction effect confirms that the combined benefit is equivalent to the sum of the benefits of each treatment alone.

As in many long-term trials, patient compliance was disappointing, with ~30% of patients attending less than half the allocated exercise sessions. Compliance with pyridostigmine was higher, but the estimate may have been inflated because it relied on patient reports only. Nevertheless, even with this level of compliance, the results are generally clinically worthwhile.

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References

- Busch AJ et al (2007) *Cochrane Database of Systematic Reviews* Issue 4.
- Jones KD et al (2006) *Health Qual Life Outcomes* 4: 67–72.
- Jones KD et al (2007) *Semin Arthritis Rheum* 36: 357–379.
- Maher CG et al (2003) *Phys Ther* 83: 713–721.
- Wolfe F et al (1990) *Arthritis Rheum* 33: 160–172.